

## Short Communication

# Pinacol coupling of aldehydes and ketones using lithium metal

BRINDABAN C. RANU,\* JYOTIRMOY DUTTA AND UMASISH JANA

Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Calcutta 700 032, India

email: oibr@mahendra.iacs.res.in; Phone: 91-33-4734971 (extn: 247); Fax: 91-33-4732805.

Received on August 29, 2000.

### Abstract

Aldehydes and ketones undergo self-coupling to produce pinacols by a simple treatment with lithium metal in THF under sonication. A good stereoselectivity in favour of *DL*-isomer has been observed.

**Keywords:** Pinacol coupling, aldehydes, ketones and lithium metal.

Recently, during a lithium-mediated addition of 1-chlorocyclohexene to acetophenone in THF, we observed a self-coupling of acetophenone to pinacol in place of the desired reaction. Our subsequent literature survey reveals only one example of lithium-mediated pinacolization of camphor in very low yield (20%).<sup>1</sup> This prompted us to revisit lithium-mediated pinacol coupling of carbonyl compounds in general. Although discovered long back, the pinacol coupling is still one of the most useful reactions for the formation of carbon–carbon bonds.<sup>2</sup> During the past few years quite a number of reagents have been developed for effecting this important transformation. These include various metals such as sodium,<sup>3a</sup> magnesium,<sup>3b</sup> aluminium,<sup>3c</sup> manganese,<sup>3d</sup> ytterbium,<sup>3e</sup> metal iodides like  $\text{SmI}_2$ ,<sup>4a</sup>  $\text{MgI}_2$ ,<sup>4b</sup>  $\text{CeI}_2$ <sup>4c</sup> as well as versatile  $\text{TiCl}_3$ -based reducing agents.<sup>5</sup> However, most of these reagents lack general applicability being satisfactory only for the aromatic aldehydes. Aliphatic aldehydes and ketones are either inert or undergo pinacolization in very low yields. In addition, some of these reagents being toxic are not environment-friendly. Thus, an efficient and general procedure using nontoxic reagent for this coupling reaction is still in demand. We have found that aldehydes as well as ketones undergo clean coupling to the corresponding pinacols when treated with lithium metal in THF under sonication.

In a typical general procedure, carbonyl compound (aldehyde or ketone, 1 mmol) in THF (5 ml) was sonicated with finely cut lithium metal (1.2 mmol) in an ultrasonic cleaning bath (150 W, 35 kHz, Julabo USR3) for a certain period of time as required to complete the reaction (TLC). The reaction mixture was then quenched with careful, dropwise addition of saturated solution of ammonium chloride and extracted with ether. Evaporation of ether followed by

**Table I**  
**Coupling of carbonyl compounds with Li metal in THF under sonication**

Entry	Carbonyl compound	Time (h)	Yield of diol (%) <sup>a</sup>	Ratio (dl/meso) <sup>b</sup>
1	Benzaldehyde	10	70 <sup>c</sup>	85:15
2	Octanal	9	75	88:12
3	Decanal	7	78	90:10
4	2-Methoxybenzaldehyde	10	78	90:10
5	3-Methoxybenzaldehyde	11	76	93:7
6	4-Methoxybenzaldehyde	15	70	98:2
7	Acetophenone	14	76	92:8
8	4-Methoxyacetophenone	15	70 <sup>c</sup>	75:25
9	4-Methylacetophenone	16	76	80:20
10	3-Pentanone	15	55	—
11	Cyclohexanone	15	60	—
12	Cycloheptanone	16	62	—
13	Cyclooctanone	14	64	—

<sup>a</sup>Yields refer to those of pure isolated products fully characterized by spectral (<sup>1</sup>H and <sup>13</sup>C NMR) data; <sup>b</sup>The ratio was determined by <sup>1</sup>H NMR analysis; <sup>c</sup>Some amount (10-15%) of alcohols corresponding to reduction were also isolated.

column chromatography of the crude product over silica gel furnished the pure product. Stirring at room temperature without sonication makes the reaction very slow; the conversion being less than 10% even after 12 h.

Several structurally varied carbonyl compounds were subjected to this procedure to produce the corresponding diols (Table I). This procedure works well for aliphatic as well as aromatic aldehydes and ketones. The yields of corresponding pinacols are in general good although some amount (10–15%) of alcohols are obtained in the case of benzaldehyde (entry 1) and *p*-methoxyacetophenone (entry 8). Aliphatic ketones are found less reactive (entries 10–13) and the yields of diols are relatively low as a considerable amount of starting materials remained unreacted even after prolonged treatment. However, the diastereoselectivity is remarkably good in all of the reactions, DL-isomer being formed predominantly or almost exclusively. The position of substituents in the aromatic ring (*o*, *m*, *p*) does not influence yields or diastereoselectivities (entries 4–6) of pinacols drastically.

In conclusion, the present procedure using lithium metal and THF provides an efficient methodology for pinacolic coupling of carbonyl compounds. The experimental simplicity, general applicability to aliphatic as well as aromatic aldehydes and ketones, mild reaction conditions, and most significantly remarkable diastereoselectivity make this procedure a practical and better alternative for this useful reaction. Further investigations to broaden the scope of this methodology and use it in natural product synthesis are under progress.

### Acknowledgements

This investigation has enjoyed financial support from the Council of Scientific and Industrial Research (CSIR), New Delhi (Grant No. 01(1504)/98). JD and UJ thank CSIR for fellowships to them.

## References

1. a. PRADHAN, S. K., THAKKER, K. R. AND MCPHAIL, A. T. *Tetrahedron Lett.*, 1987, **28**, 1813-1816.  
b. HUFFMAN, J. W., WALLACE, R. H. AND PENNINGTON, W. T. *Tetrahedron Lett.*, 1988, **29**, 2527-2530.
2. a. McMURRY, J. E. *Chem. Rev.*, 1989, **89**, 1513-1524.  
b. WIRTH, T. *Angew. Chem. Int. Ed. Engl.*, 1996, **35**, 61-63.  
c. AVALOS, M., BABIANO, R., CINTAS, P., JIMINEZ, J. L. AND PALACIOS, J. C. *Recent Res. Dev. Org. Chem.*, 1997, **1**, 159-178.
3. a. NELSON, S. F. AND KAPP, D. C. *J. Am. Chem. Soc.*, 1986, **108**, 1265-1270.  
b. ZHANG, W.-C. AND LI, C.-J. *J. Org. Chem.*, 1999, **64**, 3230-3236.  
c. BHAR, S. AND PANJA, C. *Green Chem.*, 1999, 253-255.  
d. RIEKE, R. D. AND KIM, S.-H. *J. Org. Chem.*, 1998, **63**, 5235-5239.  
e. HOU, Z., TAKAMINE, K., FUJIWARA, Y. AND TANIGUCHI, H. *Chem. Lett.*, 1987, 2061-2064.
4. a. YANADA, R., NEGORO, N., YANADA, K. AND FUJITA, T. *Tetrahedron Lett.*, 1997, **38**, 3271-3274.  
b. GRIFFIN, G. W. AND HAGER, R. B. *J. Org. Chem.*, 1963, **28**, 599-600.  
c. IMAMOTO, T., KUSUMOTO, T. HATANAKA, Y. AND YOKOYAMA, M. *Tetrahedron Lett.*, 1982, **23**, 1353-1356.
5. BANDINI, M., COZZI, P.G., MORGANTI, S. AND RONCHI, A. U. *Tetrahedron Lett.*, 1999, **40**, 1997-2000.
6. SUZUKI, H., MANABE, H., ENOKIYA, R. AND HANAZAKI, Y. *Chem. Lett.*, 1986, 1339-1340.